DSJ1&2-PR Exh 545

From: Connell, Jill
Sent: Friday, March 22, 2013 4:21 PM
To: Hernandez, Tracey
Subject: FW: composite risk assessment
Attachments: Defined Risk and Solutions -jmc 9-6-12.xlsx

From: Connell, Jill
Sent: Friday, March 22, 2013 2:09 PM
To: Patel, Sanjay
Subject: FW: composite risk assessment

From: Connell, Jill
Sent: Thursday, September 06, 2012 4:30 PM
To: Hudson, Denise; Cowan, Steven; Cook, Steve; Moes, Michael; Pelin, Kevin; Hunt, MaryMichelle (Shelly); Jiwrajka, Santosh (Sam)
Cc: Cupero, Phil; Michael Keech (mike.keech@celerantconsulting.com); Cuca, Roberto; Baker, Goff; Timothy J. Jubach (tjubach@aol.com); JimBConnolly@aol.com; Hernandez, Tracey
Subject: RE: composite risk assessment

Denise,

Tracey and I just met and updated the DEA portions of the attached file; including known fines were applicable in the evidence of risk column.

Regards,
jill

From: Hudson, Denise
Sent: Monday, September 03, 2012 3:01 PM
To: Cowan, Steven; Cook, Steve; Moes, Michael; Connell, Jill; Pelin, Kevin; Hunt, MaryMichelle (Shelly); Jiwrajka, Santosh (Sam); Hernandez, Tracey
Cc: Cupero, Phil; Michael Keech (mike.keech@celerantconsulting.com); Cuca, Roberto; Baker, Goff; Hudson, Denise; Timothy J. Jubach (tjubach@aol.com); JimBConnolly@aol.com
Subject: composite risk assessment

All,
I have put some time into the composite risk assessment based on our discussions last week. I attempted to name and describe the risks and define our evidence that these are real risks as well as the potential impact. I hope this works. I ran out of time and was not able to incorporate all the risks from the DEA assessment. **Jill or Tracey,** I was hoping you would be able to complete the chart with those risks, evidence and solutions that were identified by the team. I think this format should work. Hope the meetings this week go well. I will catch up with you later in the week.

Denise

Denise Hudson

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Produced In Native Format

INTEGRATED COMPLIANCE RISK ASSESSMENT

init item no.	Reg. Area	Risk Name	Risk description	Composite Risk	Potential impact	Evidence of Risk	Solution identified		status / comments
							Fcntl Area	Solution	
MULTIPLE AGENCIES									
7	DEA, FDA	Scales and Weighing	Lack of Scales/Weighing at key points in the process cause cross contamination and/or inaccurate tracking of CS	H	DEA actions with oversight; fines ($10,000 per incident which when multiplied by the number of incidents can be significant).	DEA observation from inspection; Endo commitment. Rite Aid was fined $5M dollars for failure to identify losses in three of their facilities in 2009		complete implementation; acquire additional scales for key areas	Project initiated. Scales needed at docks for receipt and in vault and cage. Plan being reviewed by QT DEA team and Engineering team.
8, 55	DEA, FDA	Inventory management	–Inadequate Inventory Management System prevents proper lot tracking, CS traceability; reconciliation discrepancies	H	Fines; required action with oversight; warning letter; potential for "snowball" effect.	CFR; comments by FDA and DEA during inspections; DEA observation from inspection. Express Scripts was fined $2.75M for inventory discrepancies in 2012	IT; Engin	Obtain and implement IT system to track inventory receipts through manufacturing; ability to identify inventory at stages in process by lot; traceability of all components	Procedural and IT systems; will also have benefit to productivity
10	DEA, FDA	Staff background	Hiring practices do not meet requirements (background checks, temps) and reevaluation of current employees is inadequate as not repeated once hired.	H	Fines; required action with oversight; potential for "snowball" effect.	Observation from DEA inspection; comments from past DEA visits; Uds. St. Vincent Hospital was fined $2M for failure to have measures in place to expose hidden employee theft in 2007	HR, Mfg	Add OpEx to complete full background checks; change hiring to direct hire vs. temp to full	Procedural and OpEx
12, 27, 33, 34, 46	DEA, FDA, OSHA	Dust containment	Dust containment issues across all plants cause risks for employee exposure; cross contamination; inadequate controls of PCs; inadequate management of CSs; HVAC/RECIRC- dust collectors recirc air in tablet area; material handling also increases foreign material events.	H	Injury to employees; warning letters; fines; actions required with oversight; batch failure; potential diversion, productivity losses; whistleblower	CFR; DEA comments during 2011 visit; OSHA guidelines; Teva observation resulting in WL; our data shows issues ispe baseline guide, table 4.1	Engin; Facils; Mfg; R&D	1. Dust containment project 2. Closed Transfer of materials 3. Bin blending 4. Tablet dust collectors redesigned to be single pass 5.HEPA filters implemented at each room for incoming air 6. Improve material handling	Requires significant change to facility and processes; could cause yield and productivity improvements Doorway solutions under evaluation: Airlocks, training, procedures, etc.
28	FDA, DEA	Packaging	Packaging lines are old and present certain risks due to lack of key technology: vision systems to check labels, batch and exp dates and outserts; line clearance; fill accuracy; tablets hidden on line; equipment qualification: inability to reconcile product sufficiently; Need to prepare lines to manage "track and trace" by 2015	H	FDA warning letter; required changes and timing with oversight; recalls, productivity impact, and diversion	CFR; for cause FDA inspection in 12/11; high level of complaints for short counts; FDA 483 observations; UDs, recalls, focused effort on "no place to hide" initiative as well as prior diversions resulting in employee termination and more frequent DEA inspections as well as directives on how to run our business	Eng, mfg, IT	upgrade where most cost effective and replace where needed; best solution still being evaluated	Waiting for packing line assessment report; target is to productivity benefit may accrue but is not the basis of these upgrades
DEA									
1,2,3	DEA	CS Storage	Insufficient storage in vaults, cages 1. HSV tablets 2. Distribution 3. CLT	H	Fines (10,000 per incident), Warning Letter, required action with oversight; delay in quota approvals; delays in import/export licenses, ultimately loss of license	DEA direct feedback in observations and follow up commitment by Endo	Facils; Engin	1. design/build additional space 2. begin design; build once strategy is final 3. Move CS, except Carisoprodol to HSV	1. Project initiated 2. Decision pending final manufacturing/distribution strategy, but suggest that programming and preliminary design begin now. 3. none required

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4	DEA	Mezzanine Storage	–Tablets Mezzanine storage & set-up	H	Fines, required action with oversight, loss of license	DEA regulations for Schedule II storage requirements	Engin; Facils	Immediate: 1. Restrict access, storage of CII WIP and improve security around each IBC. 2. Individual lockable rooms for each location or improved containment.	Examining opportunities to address immediately; longer term will be addressed by additional vault and cage space.
5	DEA	Lab CS Management	need improved controls for CS samples in labs	H	Fines, required action with oversight	DEA regulations for storage requirements	Quality; Facils	Central control area in lab for all scheduled product samples. Implement safe(s) and re-inforce area with mesh/cage.	Project initiated
6	DEA	Suspicious order Monitoring	Monitoring and reporting not meeting all requirements; inconsistency across Endo	H	Fines, required action with oversight; cease selling to certain accounts	DEA regulations; observation from inspection. Cardinal has a 2 yr suspension of Lakeland, FL location's DEA License. Fines ranging from $320k up to $13.25M	IT; Comm; Distn	– Design and implement improved IT system for suspicious order monitoring in distribution	
9	DEA	Customer registration	Check customer registration occasionally; inconsistency across Endo.	H	Fines of $10,000 per customer per shipments for shipping to non-reg customers	Sandoz fines ($700K)	Distn	Purchase of NTIS tapes, IT development program to compare our accounts to NTIS data, Staff to investigate outliers and/or exceptions.	Procedural; opex only
Health and Safety									
11	Safety	Emergency Response	Emergency response plan and supporting systems are inadequate	H	Inadequate response to an event; undue harm to employees	Tornedo response slow; chemical exposure in CLT; PC exposure event in HSV Tablets	EHS; Security	Develop emergency response plan and establish effective system to execute in all 4 sites	Procedural and emergency response system. - 2012 Capital plan - need OpEx to staff and complete
13, 14, 15, 19	Safety	Material movement safety	Mfg procedures and processes require excessive levels of scooping, lifting, working at heights, twisting and lifting simultaneously; Liquid tank charging; facility design in some areas presents excessive risk of slipping and falling; machine/human impact	H	Significant employee injury; foreign matter in batches; OSHA citations or fines	Safety tracking: Need data OSHA guidelines Inconsistency across Endo Visual observation and employee call outs	Eng, Facils, Mfg, Quality	1. Material transfer project. 2. Drum lifts/inverters. 3. Lifts in warehouse, mfging, and pkging. 4. Housekeeping. 5. Training. 6. Safety staircases for access to roof (Tabs and Liq). 7. Safety railings in CLT, HSV Tabs, and Liq second floor. 8. Post lift to charge blenders or material handling/transfer solns. 9. Replace fork trucks in manufacturing with hand trucks. 10. Triblender induction pump.	Tactical solutions are underway; process design is underweigh; will require engineering and R&D design of processes, validation and OpEx; Liquid chargin project initiated and is 2011 carry over project
18	Safety	Potent Compound management	Potent compounds are manufactured under conditions that do not meet OSHA guidelines	H	Employee injury; whistleblower; fines; negative publicity	OSHA requirements; internal data on exposure limits; recent LWDC	Eng, Facils, Mfg, EHS	Short term, dust containment project to minimize dust. Build PC suite in HSV tablets for PC/CS; potentially outsource other PCs; options still being evaluated	May be able to transfer equipment at Novartis to use in HSV suite
20, 21, 22	OSHA, local building codes	Combustion and Flammability	Insufficient fixtures, room and equipment design in key areas to prevent product combustibility and/or solvent flammability	H		Building codes	Facils; Engin	1. Upgrade to Class 2 Div 2 electrical fixtures where necessary (high dust areas - blending, compression, fluid bed rooms) 2. upgrade rooms and equipment for mfging processes using solvents to XP rating (HSMG, film coater)	Designs underway
Environmental									

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23, 25	EPA, NCEPA, ADEM	Environmental waste management	Storage and discharge of environmental waste are now at higher levels (Endo is high volume hazardous waste generator)	H	Fines; negative publicity; required actions and timing by authorities	RCRA guidelines; ADEM fines at Endo in 2011; NCEPA comments in inspection in 2011	EHS; Eng	Increase frequency of waste pickup (OpEx); Manage and monitor emissions more regularly (OpEx)	Waiting for completion of environ assessment report; Resource Conservation & Recovery Act targeting zero discharge
24, 26	EPA, NCEPA, ADEM	Air and Water Emissions	Air emissions seem to be within limits; waste water may require treatment in future.	M		RCRA guidelines; EPA and ADEM guidelines	EHS; Eng	TBD; continue monitoring	Waiting for completion of environ assessment.report.
FDA									
31, 32	FDA	Facility standards	Facilities do not meet current standards and pose potential for cross contamination inability to properly clean, wear, peeling; not consistent across plants; slip hazards	H	"snowball effect" resulting in forces action with oversight or warning letter; disruption due to unplanned shutdown or UDs	ispe baseline guide, table 4.1; comments made by DEA and FDA during visits	Facils; Engin	Floors: Upgrade painted floors in all plants to stone hard or equivalent. Ceilings in HSV tablets: Replace existing ceiling tiles with mylar faced, clipped down tile grds.	improvements could be completed over time, if started soon
42, 43, 44, 45	FDA, possibly DEA	Process Reliability	manufacturing processes are not always capable, robust and/or scalable resulting in process failures, stability failure, customer complaints, work-arounds, UDs, recalls, high waste and scrap	H	FARs, Recalls, excessive customer complaints, 483 observations, "snowball effect" resulting in warning letter or actions required with agency oversight, impacting quota and DEA ARCOS reports and DEA destructions	CFR - reliable processes; addressing complaints; repeatable and validated processes; appropriate equipment, current GMPs; 1/3 of recalls; fat and broken tablet FARs and recalls	R&D, Tech Ops, Eng, IT	cross functional project to develop milestone and statistically based process development and validation; PE teams to characterize key ingredients and improve problematic processes; ongoing analysis of trends to identify areas for focus; complete any remedial equipment qualification and modernize equipment where qualification cannot be reliably completed; design control procedures to ensure qualification is done for all future new products and any changes	Equipment (tablet inspection post compression for high risk processes), new product process development and current product process improvement are urgent needs Presses with modern controls and improvement of processes that are not currently marketed could be delayed to outer years involves OpEx for consultants and technical staff as well as capital for equipment and validation
47, 48, 50, 51, 52	FDA	Quality Systems	Certain Manufacturing and Quality systems should be improved to enable statistical analysis of trends, improved timing to investigate and close events, reduce frequency of events, anticipate recurrence and evaluate effectiveness of CAPAs	H		CFR; number and time to close UDs and CAPAs. FDA comments during inspections; observations in Novartis, Sandos and Teva warning letters	HR, Mfg, IT, Quality	Consulting support to develop training program (on-line and hands-on), staff to manage and track results, LMS to enable on-line training Focused compliance group to increase utilization of Trackwise and LIMS to analyze trends, identify risk areas and cause improvement	Process, procedure and some IT investments; build capabilities in statistical analysis and quality system design
49	FDA	Supplier Management	Current staffing is designed to manage CMOs, key API suppliers and brand Pharma suppliers; over 300 additional suppliers provide ingredients to Qualitest and their sources of materials, methods and trends are not effectively overseen	H	FARs, Recalls, 483 observations, "snowball effect" leading to warning letter or required actions with agency oversight	CFR; recent 483s that identify marketing company as accountable; external quality consultants emphasizing need to oversee suppliers closely and all the way back to origin of materials	SC procurement; mfg, IT, R&D	continue investment in consultant support and BSA team to complete assessments and improvement plans; staff Qualitest Materials Mgmt and Quality to oversee, measure and audit suppliers using a risk-based approach	Process/procedural.
53	FDA	Equipment Cleaning	Equipment cleaning, especially processing equipment is not effective and often fails visual test; multiple cleans indicates an ineffective and not validated process	H	FDA 483; "snowball effect" resulting in more serious agency actions; cross-contamination or product failure post-marketing	CFR; recent issues at Novartis in mfg Opana ER and MSER; Warning letter to Sandoz	Eng, Tech Ops, R&D	Acquire portable clean-in-place systems for blenders, film coates and HSMGs; revalidate cleaning with this equipment to establish reliable and repeatable cleaning	CIP skid with spray balls and jets
30	FDA	Facility Walls	Walls to not meet current standard of "smooth, washable surface"; chance of residue; paint peeling	M	483 observation	ispe baseline guide, table 4.1;		no change at this time	

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35, 36	FDA	GMP Space separation	separation of clean space vs.non GMP space does not meet current standards in several areas presenting risk of cross contamination; environmental burden;	M	483 observation; some chance of "snowball effect"	ispe baseline guide, table 4.1;	Facils; Engin	Airlocks and clean zone transition for GMP risk. Cardreaders and restricted access for DEA risk. Replace spiral with GMP stairs or elevator.	Solutions under evaluation.
37, 38, 41	FDA		Oven in HSV tablets opens into corridor; spray solution prep is done in open tanks; potential for micro contamination in purified water	M	483 observation; UDs, some chance of "snowball effect"	CFR	Eng, Facils	Enclose access to oven and add tray dumping capability. Replace open tanks with closed vessels; add ozonator to water system	
29, 39	FDA	Quality facility improvements	lack of back up stability chambers; insufficient controls in label storage	M	need to find immediate alternative if stability chambers fail; serious GMP violation if can't maintain stability; 483 observation possible for label control	CFR	Quality Facils	Investigate outsource alternative; install additional storage; Install better control cages and improve procedures	Solutions should be put in place during other improvements or could be delayed to out years

Risk Categories:

H - high risk, must address - Level 1 urgency

M - moderate risk, should evaluate solutions but not urgent at this time - Level 2 urgency

L - low risk, consider potential solutions - not included in this analysis

BRAINSTORM SOLUTIONS	Strategy (S) or Risk (R)									
Facilities	**S or R**	**Risk Solved**	**Equipment and Technology**	**Risk Solved**	**Process Improvement**	**Risk Solved**	**Information Systems**	**Risk Solved**	**People**	**Risk Solved**
Packaging			Bin blend and feed equipment from above				Bar code			
Packaging COE for HSV in distribution center	S		QC expansion							
Build Packaging COE and maintain distribution center	S		Move to aqueous based solutions (away from solvents)							
CMO packaging of non-controlled substances	S		Improved Material Handling							
Potent compound packaging in COE	R	Handling potent compounds	Dust Containment Solutions and closed transfers							
Keep packaging as-is (baseline case) Impement Track and Trace (does it fit?)	R	Track & trace	Improved cleaning solutions							
Move CLT packaging into HSV COE	S		Packaging tote feeding							
Single site DEA by linking packaging COE in DC to MFG	S		In process scales							
HPC			Hi shear granulation improvements							
Outsource HPC	R	Handling potent compounds	Mistake proofing using technology							
Brownfield HPC solution	R	Handling potent compounds	Packaging technology							
Build internal HPC Capability	R	Handling potent compounds	NPI							
Charlotte										
Non-controlled and bulk mfg only	S									
Charlotte Shutdown	S									
Minimize investment										
3-5 year capped capacity										
Find a new site to replace										
Huntsville Tablets										
Fill to capacity	S									
Facilities upgrades to mitigate risk	R	SEE DEFINED RISKS								
Facilities upgrades to improve flow	S									
Reconfigure mezzanine	R	Controlled substance handling & FDA compliance								
Solvent Capability	R	EH&S								
Distribution Center										
Huntsville Expansion	S									
Huntsville Expansion + 2 new sites	S									
2-3 new sites (internal, partner or outsource)	S									
QC expansion	S									
Security Access	R	**DEA security**								
Define Scope of potent compounds	R	Handling potent compounds								

Scenarios to consider

1	Baseline Case	Get what we can out of what we have: must expand warehouse by 12/31, all controlled in HSV. Need to model mods for keeping carisoprodol in CLT)	
2	Packaging COE in DC, Paul option #1	Absorb Charlotte and HSV packaging in COE, pull bulk through plants	Reduces labor, gives flexibility to bring outsourced pcg in house
2.1	Right size COE with some packaging at CMO		
2.2	All controlled in HSV, all pckg in COE		
3	High Potent Compounds		
3.1	All in HSV		
3.2	PC Suite, just C2/s & outsource balance	Jeff proposal	
3.3	Brownfield HPC and move	Known plant	

Minimal investment in HSV/CLT to address risk

10,000,000,000	0.001	$10,000,000.00